Howard Hughes Medical Institute
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Centers for Disease Control and Prevention
Division of Select Agents and Toxins
1600 Clifton Road, MS E-79
Atlanta GA 30333

RE: Comments on the reconstructed replication competent forms of the 1918 pandemic influenza virus containing any portion of the coding regions of all eight gene segments

Dear Colleagues:

The Intragovernmental Select Agents and Toxins Technical Advisory Committee (ISATTAC) was correct in concluding that the reconstructed 1918 influenza viruses could pose an immediate and severe threat to public health and, as such, should be regulated.

With respect to the issue of possible current immunity to 1918 virus, the same researchers who reconstructed the 1918 virus reported last year that only individuals born before or shortly after the 1918 pandemic exhibit detectable HA and virus-neutralizing antibody titers against 1918 HA. ["HI and virus neutralizing (VN) antibodies to 1918 recombinant and Sw/Iowa/30 viruses in human sera were present among individuals born before or shortly after the 1918 pandemic....Antigenic analysis by hemagglutination inhibition (HI) tests with ferret and chicken H1N1 antisera demonstrated that the 1918 recombinant viruses...differed from H1N1 viruses isolated since 1930"; PNAS 101:3166, 2004]

With respect to the issue of possible effectiveness of current vaccines against the 1918 virus, the same researchers who reconstructed the 1918 virus reported last year that there are no influenza vaccines currently approved and available that could be used as effective prophylactic measures if the 1918 virus is re-introduced into human populations. ["There are no influenza vaccines currently available that could efficiently be used as prophylactic measures if a 1918-like virus reemerges"; PNAS 101:3166, 2004]

Therefore, I wish to express my strong support for the decision to add 1918 influenza viruses with all eight 1918 genes to the select-agent list.

Furthermore, I wish to recommend the following additional regulatory actions

- Add 1918 influenza viruses containing at least one 1918 gene to the select-agents list.
  I make this recommendation since viruses having even one 1918 gene exhibit exceptional lethality (Nature 431:703, 2004; PNAS 101:3166, 2004).

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- Add nucleic acids containing at least one 1918 gene to the select-agents list.
  I make this recommendation since viruses having at least one 1918 gene readily can be prepared starting form nucleic acids (Nature 431:703, 2004; PNAS 101:3166, 2004; Science 310:77, 2005). No specialized training is required, no specialized equipment is required, and minimal time and cost are required. Possession of nucleic acids containing at least one 1918 gene must be considered tantamount to possession of viruses containing at least one 1918 gene.]

- Add work with any of the above to the "Restricted Experiments" under the select-agents rule.
  I make this recommendation since I believe that national-level review and approval should be required before initiating work with viruses or nucleic acids containing at least one 1918 gene.

- Require biosafety level 4 (BSL-4) containment for work with any of the above.
  I make this recommendation since I believe that the highest level of biosafety containment should be required for work with viruses or nucleic acids containing at least one 1918 gene.

I appreciate the opportunity to comment on regulation of reconstructed 1918 influenza viruses under the select-agents rule. Thank you in advance for your attention.

Sincerely,

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